LANDRY-GUILLAIN-BARRE SYNDROME – THE ISOLATION OF AN ECHOVIRUS TYPE 6*

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THE Landry-Guillain-Barré syndrome is a well-recognized clinical entity, characterized by involvement of the central nervous system with varying degrees of motor and sensory nerve disturbance. A frequent accompaniment is a rise in the level of cerebrospinal fluid protein unassociated with a similar rise in the number of white blood cells in the spinal fluid; this dissociation is an important diagnostic criterion.

The existence of the syndrome as a distinct entity has been disputed;[1] it has been reported to occur in association with a number of diseases of quite divergent etiology on the basis of an allergic phenomenon.[3] These have included tuberculous meningitis,[2] Cushing's disease,[4] infectious mononucleosis,[5] diphtheria,[1] and multiple myeloma.[6]

Many features of the syndrome suggest a viral etiology; the lack of a rise in the cerebrospinal fluid white cell count, however, is difficult to equate with a viral infection of the central nervous system. It could be postulated that a virus which had no primary cytopathogenic effect on nerve tissue proper could produce œdema of the brain stem, spinal cord, spinal nerve roots, and hyperæmia of the meninges that results in the symptoms characteristic of this entity.

The purpose of this communication is to report the isolation of an Echovirus, type 6, from the fæces and cerebrospinal fluid of a ten-year-old boy with clinical and laboratory findings that conform to the criteria laid down for the diagnosis of Landry-Guillain-Barré syndrome.[2]

The patient, a ten-year-old boy, was quite well until July 27, 1959; on this day he complained of a sore throat, and his mother observed a swelling of the anterior neck on both sides. The illness appeared to be a relatively minor one as there was no detectable fever and the patient recovered completely in two or three days. Seven days later, on August 3, he complained of general fatigue, as well as numbness and tingling of the fingers and toes. His father observed that the left upper eyelid was drooping. The patient still had no fever and did not complain of headache or muscle pain. On August 4, the right upper eyelid was drooping and during the remainder of this day the patient developed progressive muscular weakness extending proximally in all limbs. At this time the patient was admitted to the Calgary General Hospital.

On admission there was no fever and no complaint of headache or stiff neck; there were complaints, however, of paræsthesiæ of the fingers and toes. Examination on this date revealed bilateral seventh nerve weakness, left fifth motor nerve weakness and weakness of the left lateral rectus muscle. The patient's general muscle power was reduced in a symmetrical manner, which was more evident proximally than peripherally. Examination revealed no objective change in sensation; he was areflexic except for the abdominal and plantar responses. On August 6, the patient developed marked respiratory distress. An emergency tracheotomy was performed, and examination now revealed paralysis of the muscles supplied by the ninth and tenth cranial nerves. His general condition deteriorated rather suddenly overnight.

On the afternoon of August 6, he was almost completely paralyzed and was transferred to a negative-pressure tank-type respirator. On this same day hydrocortisone (as Solu-Cortef) therapy was begun, and 200 mg. was given intravenously per day, in divided doses. His condition remained much the same for the next four days. On August 11 signs of improvement began with the return of function to the ninth and tenth cranial nerves; this was followed shortly by an improvement in function of the other cranial nerves. With this improvement, the steroid dosage was gradually reduced, and 21 days after admission, was discontinued. His improvement from this point onward was as rapid as his previous deterioration. By August 24 the patient had recovered all muscle power except for some residual paralysis associated with the sixth cranial nerve; this returned to normal by August 30 when a general muscle grading test showed no abnormality apart from some residual lateral rectus weakness. He was therefore discharged home. On October 5 a complete physical examination revealed no abnormality.

Previous history was not unusual; the boy had chickenpox and measles in childhood without complications. He had been vaccinated for smallpox with no unusual results. Salk poliomyelitis vaccine had been administered one year previously and all dosages were given at the correct intervals. He gave no history of recurrent attacks of infection or of unusual illness in the family.

Laboratory findings on August 5, the date of admission to hospital, showed the cerebrospinal fluid to have a pressure of 110 mm. of water; there were fewer than 5 cells/c.mm., total protein value was 16 mg. %, sugar was 80 mg. % and chlorides were 730 mg. %. The peripheral white cell count was 7600 cells/c.mm., and the differential count normal. Sedimentation rate was 4 mm./hour. On August 29, lumbar puncture was repeated and the pressure was 120 mm. of water. There were fewer than 5 cells/c.mm., the protein had now increased to 145 mg./100 ml., the sugar was 64 mg./100 ml., and the chlorides were 740 mg./100 ml.

VIROLOGICAL INVESTIGATIONS

Two specimens of fæces were received in the virus laboratory in Winnipeg, on August 10, along with one specimen of blood and a sample of cerebrospinal fluid. A cytopathogenic agent was isolated from one specimen of fæces and from the cerebrospinal fluid after 48 hours' incubation of the specimens on monkey-kidney and human-amnion cell cultures. The agent was subsequently identified by neutralization tests as a type 6 Echovirus. On August 25, a second specimen of blood was received, representing the convalescent sample;

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neutralization tests were carried out on both the acute and convalescent sera against the virus isolated from the patient as well as against a stock Echovirus type 6. The first serum had a neutralization titre of 1:4 against both viruses, and the second serum a titre of 1:8. In view of this low titre and the lack of demonstration of a significant increase in antibodies in the convalescent serum, both sera were tested for antibodies to Poliovirus type 1 and to herpes simplex; the majority of persons at this age would demonstrate quite a high titre of antibodies to these two common viruses despite steroid therapy. The titre against poliovirus type 1 was 1:8 in both sera and titre to herpes simplex was 1:4. This low concentration of antibodies paralleled the antibodies for the Echovirus type 6, and raised the question of a serum protein abnormality, i.e., hypogammaglobulinæmia. Serum proteins were examined by hanging paper strip electrophoresis, using the Spino apparatus with barbital buffer at pH 8.6 and ionic strength 0.05; the staining was carried out with bromphenol blue. This revealed that the alpha-1 globulins were absent from both specimens and that the gamma globulins were below normal. In both the acute and convalescent sera, the beta globulin fraction was increased, consistent with the acute stage of an active infection (Fig. 1). These results were repeated by a different laboratory using the same technique, and similar results were obtained. Control sera stored in a similar manner were subjected to electrophoresis. These controls were obtained from boys in the same age group and both showed the alpha-1 fraction to be present.

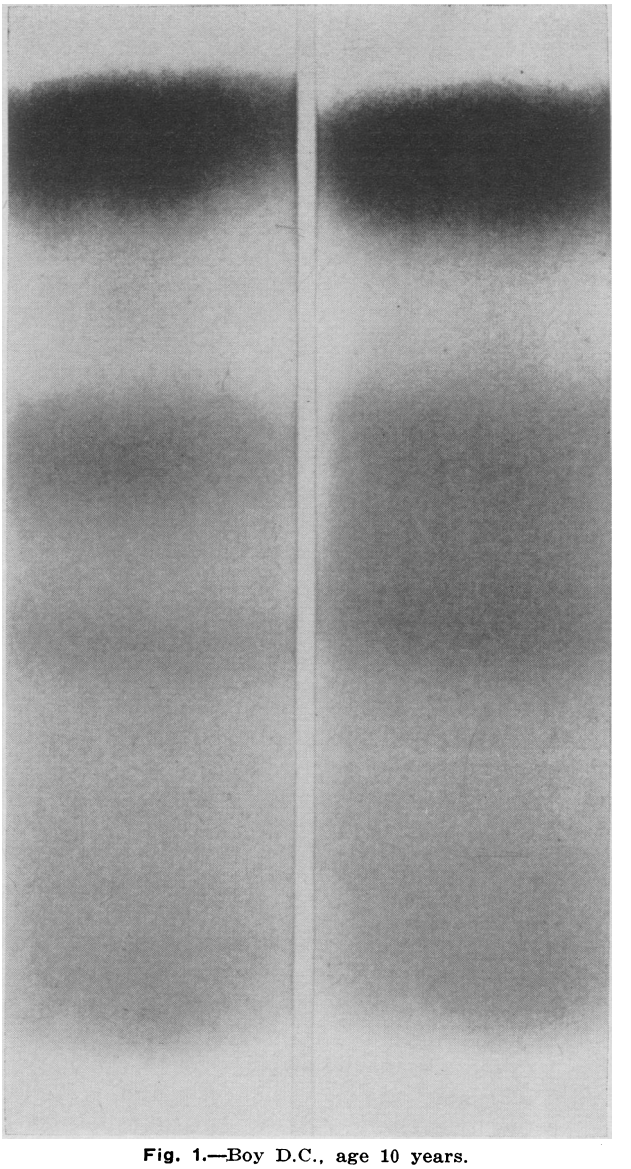

Fig. 1.—Boy D.C., age 10 years.

1. Acute		2. Convalescent	
Total Protein	8.2 g. %	Total Protein	6.5 g. %
Albumin	4.3 g. % (52%)	Albumin	3.58 g. % (55%)
α-1 Globulin	Missing	α-1 Globulin	Missing
α-2 Globulin	1.0 g. % (12%)	α-2 Globulin, β Globulin	2.13 g. % (32.8%)
β Globulin	2.3 g. % (28%)		
γ Globulin	0.6 g. % (8%)	γ Globulin	0.79 g. % (12.1%)

DISCUSSION

There is some difference of opinion over precisely what constitutes the Landry-Guillain-Barré syndrome. Lewey[7] considers the term a useful one to designate the various polyneuropathies despite the fact that there is some diversity of opinion as to exactly what constitutes the syndrome. Haymaker and Kernohan,[8] following an analysis of 50 fatal cases, consider the name to be useful in labelling cases of primary radiculopathy with or without sensory changes. Merrill and Fredrickson,[2] in an excellent study of 37 cases at the Vanderbilt Poliomyelitis Respiratory and Rehabilitation Center, confined their investigations to cases fulfilling the following criteria: the presence of paralysis, the absence of cultural and serological evidence of poliomyelitis as well as of other specific diseases, an increase in the amount of spinal fluid protein at some time during the course of the disease, and a normal number of white blood cells in the spinal fluid throughout the disease. Most cases recover spontaneously with little or no sequelæ.[9] The authors think that there is good evidence for classifying the case presented as one of Landry-Guillain-Barré syndrome.

The isolation of an Echovirus type 6 from the spinal fluid is highly significant and in all probability indicates this to be the etiology of the disease in this particular patient. The lack of supporting evidence by way of an increasing antibody titre in the serum during the course of the disease may well have been due to the steroid therapy given. The severity of this particular virus infection may have been associated with the abnormal serum protein pattern, as shown by paper electrophoresis, of both the acute and convalescent sera. Although the part played by gamma globulin in many bacterial infections is fairly clear, the relation of the various protein fractions to viral immunity is largely unknown. It has been considered that not all viral antibodies are represented by the gamma globulin fraction; this is supported by the lack of occurrence of an excessive number of virus infections in patients with hypogammaglobulinæmia or agammaglobulinæmia.

Although it is recognized that steroid therapy can reduce abnormally high alpha-1 globulins to normal,[10, 11] the complete absence of the alpha-1 globulin in the acute and convalescent sera of this patient is interesting; this raises the question whether serum fractions other than gamma globulin may play a part in viral immunity. Preliminary investigations indicate that this deficiency of alpha-1 globulin fraction may be an artefact, such as denaturation of lipoproteins or glycoproteins. Its significance, however, is not apparent from an appraisal of the present literature. As a result we have initiated an investigation into the part played by the various serum protein fractions, particularly the alpha-1 fraction, in the immunity associated with viral infections.

SUMMARY

A case of Landry-Guillain-Barré syndrome is reported in which an Echovirus type 6 was isolated both from the fæces and the cerebrospinal fluid. A significant rise in antibody titre to this virus did not occur in the convalescent serum and may be explained by the steroid therapy given. The electrophoretic pattern of both sera was abnormal, however, and there was a deficiency of antibodies to both poliovirus type 1 and the herpes simplex virus. The significance of these findings is discussed and it is felt that the syndrome may be caused by a variety of viruses which, under normal circumstances, are not primarily cytopathogenic to the cells of the central nervous system and therefore do not produce irreversible damage.

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RÉSUMÉ

On rapporte le cas d'un malade présentant un syndrome de Landry-Guillain-Barré et chez qui on isola un virus ECHO type 6 des selles et du liquide céphalo-rachidien. La thérapie aux stéroïdes peut expliquer l'absence d'élévation du taux des anticorps pendant la convalescence. L'électrophorèse montra un sérum anormal dans lequel il n'y avait aucun anticorps au virus de l'herpès et de la poliomyélite type I. L'importance de ces constatations vient de ce que ce syndrome pourrait être causé par plusieurs virus qui normalement ne sont pas cytopathogènes du système nerveux central. Comme ils n'y accèdent que par accident, pour ainsi dire, les lésions qu'ils produisent ne sont pas irrévérsibles.

SCOLIOSIS: DIAGNOSIS AND NATURAL HISTORY*

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LATERAL CURVATURE of the spine in childhood is one of the most perplexing and least understood deformities that one encounters in pædiatric orthopædic surgery. A review of our experience over the past 15 years, which includes 160 spine fusions, might be of some help to the physician and surgeon faced with the problem of curvature in a growing child. Although the vast majority of cases of scoliosis are either idiopathic or paralytic in nature, there are certain other well recognized forms of scoliosis which should be included in a comprehensive survey of the subject.

Most curves can be classified according to age. Thus we have neonatal scoliosis with normal vertebræ; congenital scoliosis due to anomalies of the vertebræ; infantile or juvenile idiopathic scoliosis; paralytic scoliosis; scoliosis due to vertebral tumours or disease; and idiopathic or adolescent scoliosis. To further our knowledge of scoliosis an inquiry into the diagnosis and natural history of these various curvatures is most instructive.

CONGENITAL SCOLIOSIS

Congenital scoliosis is recognized on x-ray examination and often is an incidental finding on radiographs taken for some other reason. The classical type of congenital scoliosis is a hemivertebra, which in certain areas of the spine produces very little deformity with growth, and in other areas of the spine may produce deformity that warrants prevention. The lumbar area seems to develop a progressive curvature more often than other parts of the spine (Fig. 1). In congenital scoliosis there may be fusion of pedicles or lamina on one side, producing curvature or multiple malformations including spina bifida.

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